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| <u>L6</u> | etoposide and l4 | 65 | <u>L6</u> |
| <u>L5</u> | L4 and methotrexate | 0 | <u>L5</u> |
| <u>L4</u> | LDL adj (Apo B receptor) | 1561 | <u>L4</u> |
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☐ 1. Document ID: US 6670452 B2

L9: Entry 1 of 15

File: USPT

Dec 30, 2003

US-PAT-NO: 6670452

DOCUMENT-IDENTIFIER: US 6670452 B2

TITLE: Non-naturally occurring lipoprotein particle

DATE-ISSUED: December 30, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|--------------------------------|------------|-------|----------|---------|
| <u>Halbert</u> ; Gavin William | Jordanhill | | | GB |
| Owens; Moira Doreen | Shawlands | | | GB |
| Baillie; George | Kilmarnock | | | GB |

US-CL-CURRENT: 530/359; 435/7.1, 530/350, 536/23.5

| | | | | | | | | | | | | |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|--------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWC | Draw D |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|--------|

☐ 2. Document ID: US RE37891 E

L9: Entry 2 of 15

File: USPT

Oct 22, 2002

US-PAT-NO: RE37891

DOCUMENT-IDENTIFIER: US RE37891 E

TITLE: Target and background capture methods with amplification for affinity assays

DATE-ISSUED: October 22, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|----------------------------|---------|-------|----------|---------|
| Collins; Mark L. | Holden | MA | | |
| <u>Halbert</u> ; Donald N. | Milford | MA | | |
| King; Walter | Maynard | MA | | |
| Lawrie; Jonathan M. | Milford | MA | | |

US-CL-CURRENT: 435/6; 435/15, 435/174, 435/5, 435/7.1, 435/91.2, 536/24.3,
536/24.32, 536/24.33, 536/25.4

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|
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☐ 3. Document ID: US 6331542 B1

L9: Entry 3 of 15

File: USPT

Dec 18, 2001

US-PAT-NO: 6331542

DOCUMENT-IDENTIFIER: US 6331542 B1

TITLE: Protease inhibitors

DATE-ISSUED: December 18, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|----------------------------|-----------------|-------|----------|---------|
| Carr; Thomas Joseph | Phoenixville | PA | | |
| Desjarlais; Renee Louise | St. Davids | PA | | |
| Gallagher; Timothy Francis | Harleysville | PA | | |
| Halbert; Stacie Marie | Harleysville | PA | | |
| Oh; Hye-Ja | Exton | PA | | |
| Thompson; Scott Kevin | Phoenixville | PA | | |
| Veber; Daniel Frank | Ambler | PA | | |
| Yamashita; Dennis Shinji | King of Prussia | PA | | |
| Yen; Jack Hwekwo | Malvern | PA | | |

US-CL-CURRENT: 514/237.8; 514/332, 514/357, 514/423, 514/482, 514/483, 514/590,
544/162, 546/265, 546/332, 548/531, 560/13, 560/159, 560/22, 560/25, 564/35

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|

☐ 4. Document ID: US 6284777 B1

L9: Entry 4 of 15

File: USPT

Sep 4, 2001

US-PAT-NO: 6284777

DOCUMENT-IDENTIFIER: US 6284777 B1

TITLE: Carbohydrazide protease inhibitors

DATE-ISSUED: September 4, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|-----------------------|--------------|-------|----------|---------|
| Halbert; Stacie Marie | Harleysville | PA | | |
| Thompson; Scott Kevin | Phoenixville | PA | | |

US-CL-CURRENT: 514/332; 514/357, 514/482, 514/590, 546/265, 546/332, 560/159,
560/22, 564/35

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMC | Draw De |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|---------|
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☐ 5. Document ID: US 6265176 B1

L9: Entry 5 of 15

File: USPT

Jul 24, 2001

US-PAT-NO: 6265176

DOCUMENT-IDENTIFIER: US 6265176 B1

TITLE: Dot immunoassay on plastic sheets

DATE-ISSUED: July 24, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---------------------|-------|-------|----------|---------|
| Lin; Tsue-Ming | Miami | FL | | |
| Halbert; Seymour P. | Miami | FL | | |

US-CL-CURRENT: 435/7.92; 422/56, 422/57, 427/2.11, 435/5, 435/7.94, 435/7.95, 435/970, 435/975, 436/518, 436/531, 436/809

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMC | Draw De |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|---------|
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☐ 6. Document ID: US 6232342 B1

L9: Entry 6 of 15

File: USPT

May 15, 2001

US-PAT-NO: 6232342

DOCUMENT-IDENTIFIER: US 6232342 B1

TITLE: Protease inhibitors

DATE-ISSUED: May 15, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|----------------------------|-----------------|-------|----------|---------|
| Carr; Thomas Joseph | Phoenixville | PA | | |
| Desjarlais; Renee Louise | St. Davids | PA | | |
| Gallagher; Timothy Francis | Harleysville | PA | | |
| Halbert; Stacie Marie | Harleysville | PA | | |
| Oh; Hye-Ja | Exton | PA | | |
| Thompson; Scott Kevin | Phoenixville | PA | | |
| Veber; Daniel Frank | Ambler | PA | | |
| Yamashita; Dennis Shinji | King of Prussia | PA | | |
| Yen; Jack Hwekwo | Malvern | PA | | |

US-CL-CURRENT: 514/524; 514/602, 558/390, 564/82

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMC | Draw De |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|---------|
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☐ 7. Document ID: US 5998470 A

L9: Entry 7 of 15

File: USPT

Dec 7, 1999

US-PAT-NO: 5998470

DOCUMENT-IDENTIFIER: US 5998470 A

TITLE: Protease inhibitors

DATE-ISSUED: December 7, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|-------------------------------|--------------|-------|----------|---------|
| <u>Halbert</u> ; Stacie Marie | Harleysville | PA | | |
| Thompson; Scott Kevin | Phoenixville | PA | | |
| Veber; Daniel Frank | Ambler | PA | | |

US-CL-CURRENT: 514/482; 530/300, 530/331, 560/158

| | | | | | | | | | | | | |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Drawings |
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☐ 8. Document ID: US 5955492 A

L9: Entry 8 of 15

File: USPT

Sep 21, 1999

US-PAT-NO: 5955492

DOCUMENT-IDENTIFIER: US 5955492 A

TITLE: Carboxylic acid indole inhibitors of chemokines

DATE-ISSUED: September 21, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|----------------------------|-----------------|-------|----------|---------|
| Thompson; Scott K. | Phoenixville | PA | | |
| <u>Halbert</u> ; Stacie M. | Harleysville | PA | | |
| Widdowson; Katherine L. | King of Prussia | PA | | |

US-CL-CURRENT: 514/419; 514/382, 514/784, 514/826, 514/863, 548/250, 548/252,
548/254, 548/490, 548/491, 548/494, 549/440, 562/405, 562/466, 562/468

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|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Drawings |
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☐ 9. Document ID: US 5750338 A

L9: Entry 9 of 15

File: USPT

May 12, 1998

US-PAT-NO: 5750338

DOCUMENT-IDENTIFIER: US 5750338 A

**** See image for Certificate of Correction ****

TITLE: Target and background capture methods with amplification for affinity assays

DATE-ISSUED: May 12, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---------------------|---------|-------|----------|---------|
| Collins; Mark L. | Holden | MA | | |
| Halbert; Donald N. | Milford | MA | | |
| King; Walter | Maynard | MA | | |
| Lawrie; Jonathan M. | Milford | MA | | |

US-CL-CURRENT: 435/6; 435/174, 435/5, 435/7.1, 435/91.2, 536/24.3, 536/24.32, 536/24.33

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|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|--------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMIC | Draw D |
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☐ 10. Document ID: US 5684032 A

L9: Entry 10 of 15

File: USPT

Nov 4, 1997

US-PAT-NO: 5684032

DOCUMENT-IDENTIFIER: US 5684032 A

TITLE: Compounds

DATE-ISSUED: November 4, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|-----------------------|--------------|-------|----------|---------|
| Elliott; John Duncan | Wayne | PA | | |
| Leber; Jack Dale | Doylestown | PA | | |
| Thompson; Scott Kevin | Phoenixville | PA | | |
| Halbert; Stacie Marie | Harleysville | PA | | |

US-CL-CURRENT: 514/414; 514/419, 548/454, 548/491

| | | | | | | | | | | | | |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|--------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMIC | Draw D |
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| <u>L5</u> | L4 and methotrexate | 0 | <u>L5</u> |
| <u>L4</u> | LDL adj (Apo B receptor) | 1561 | <u>L4</u> |
| <u>L3</u> | L2 and (U937 cells) | 13915 | <u>L3</u> |
| <u>L2</u> | L1 and RPMI | 13923 | <u>L2</u> |
| <u>L1</u> | foetal calf serum or fetal calf serum | 100214 | <u>L1</u> |

END OF SEARCH HISTORY

DOCUMENT-IDENTIFIER: US 6831105 B2

TITLE: Compositions comprising ether compounds and pharmaceutical uses therefor

Brief Summary Text (12):

Primarily, the liver takes up and degrades circulating cholesterol to bile acids, which are the end products of cholesterol metabolism. The uptake of cholesterol-containing particles is mediated by LDL receptors, which are present in high concentrations on hepatocytes. The LDL receptor binds both apo E and apo B-100 and is responsible for binding and removing both IDL and LDL from the circulation. IN addition, remnant receptors are responsible for clearing chylomicrons and VLDL remnants i.e., IDL). However, the affinity of apo E for the LDL receptor is greater than that of apo B-100. As a result, the LDL particles have a much longer circulating life span than IDL particles; LDL circulates for an average of two and a half days before binding to the LDL receptors in the liver and other tissues. High serum levels of LDL, the "bad" cholesterol, are positively associated with coronary heart disease. For example, in atherosclerosis, cholesterol derived from circulating LDL accumulates in the walls of arteries. This accumulation forms bulky plaques that inhibit the flow of blood until a clot eventually forms, obstructing an artery and causing a heart attack or stroke.

Brief Summary Text (13):

Ultimately, the amount of intracellular cholesterol liberated from the LDL controls cellular cholesterol metabolism. The accumulation of cellular cholesterol derived from VLDL and LDL controls three processes. First, it reduces the cell's ability to make its own cholesterol by turning off the synthesis of HMGCoA reductase, a key enzyme in the cholesterol biosynthetic pathway. Second, the incoming LDL-derived cholesterol promotes storage of cholesterol by the action of ACAT, the cellular enzyme that converts cholesterol into cholesteryl esters that are deposited in storage droplets. Third, the accumulation of cholesterol within the cell drives a feedback mechanism that inhibits cellular synthesis of new LDL receptors. Cells, therefore, adjust their complement of LDL receptors so that enough cholesterol is brought in to meet their metabolic needs, without overloading (for a review, see Brown & Goldstein, In, The Pharmacological Basis Of Therapeutics, 8th Ed., Goodman & Gilman, Pergaman Press, NY, 1990, Ch. 36, pp. 874-896).

Brief Summary Text (14):

High levels of apo B-containing lipoproteins can be trapped in the subendothelial space of an artery and undergo oxidation. The oxidized lipoprotein is recognized by scavenger receptors on macrophages. Binding of oxidized lipoprotein to the scavenger receptors can enrich the macrophages with cholesterol and cholesteryl esters independently of the LDL receptor. Macrophages can also produce cholesteryl esters by the action of ACAT. LDL can also be complexed to a high molecular weight glycoprotein called apolipoprotein(a), also known as apo(a), through a disulfide bridge. The LDL-apo(a) complex is known as Lipoprotein(a) or Lp(a). Elevated levels of Lp(a) are detrimental, having been associated with atherosclerosis, coronary heart disease, myocardial infarction, stroke, cerebral infarction, and restenosis following angioplasty.

Brief Summary Text (31):

The statins are inhibitors of cholesterol synthesis. Sometimes, the statins are used in combination therapy with bile-acid-binding resins. Lovastatin (MEVACOR, Merck & Co., Inc.), a natural product derived from a strain of *Aspergillus*; pravastatin (PRAVACHOL, Bristol-Myers Squibb Co.); and atorvastatin (LIPITOR, Warner Lambert) block cholesterol synthesis by inhibiting HMGCoA, the key enzyme involved in the cholesterol biosynthetic pathway. Lovastatin significantly reduces serum cholesterol and LDL-serum levels. It also slows progression of coronary atherosclerosis. However, serum HDL levels are only slightly increased following lovastatin administration. The mechanism of the

LDL-lowering effect may involve both reduction of VLDL concentration and induction of cellular expression of LDL-receptor, leading to reduced production and/or increased catabolism of LDL. Side effects, including liver and kidney dysfunction are associated with the use of these drugs.

Drawing Description Text (18):

FIG. 17 shows the effect on the serum lipoprotein cholesterol profile of LDL receptor deficient mice following seven daily treatments with Compound A.

Detailed Description Text (256):

The present compositions can be administered together with treatment with irradiation or one or more chemotherapeutic agents. For irradiation treatment, the irradiation can be gamma rays or X-rays. For a general overview of radiation therapy, see Hellman, Chapter 12: Principles of Radiation Therapy Cancer, in: Principles and Practice of Oncology, DeVita et al., eds., 2nd. Ed., J.B. Lippencott Company, Philadelphia. Useful chemotherapeutic agents include methotrexate, taxol, mercaptopurine, thioguanine, hydroxyurea, cytarabine, cyclophosphamide, ifosfamide, nitrosoureas, cisplatin, carboplatin, mitomycin, dacarbazine, procarbazine, etoposides, campathecins, bleomycin, doxorubicin, idarubicin, daunorubicin, dactinomycin, plicamycin, mitoxantrone, asparaginase, vinblastine, vincristine, vinorelbine, paclitaxel, and docetaxel. In a specific embodiment, a composition of the invention further comprises one or more chemotherapeutic agents and/or is administered concurrently with radiation therapy. In another specific embodiment, chemotherapy or radiation therapy is administered prior or subsequent to administration of a present composition, preferably at least an hour, five hours, 12 hours, a day, a week, a month, more preferably several months (e.g., up to three months), subsequent to administration of a composition of the invention.

Detailed Description Text (307):

10. Example: Effect of Compound A on Lipoprotein Cholesterol Profile in LDL Receptor-Deficient Mice

Detailed Description Text (308):

Homozygous familial hypercholesterolemia is a rare human disease (.about.1/1,000,000) characterized by absent or defective LDL receptors, markedly elevated serum LDL cholesterol levels and very early and severe onset of atherosclerosis. The more common form of this disease in humans, heterozygous familial hypercholesterolemia, occurs in about one in every 500 humans. Patients with the heterozygous form of this disease also present with elevated LDL levels and early onset of atherosclerosis.

Detailed Description Text (309):

The effect of Compound A on LDL levels in a murine model of homozygous familial hypercholesterolemia (Ishibashi et al., 1993, J. Clin. Invest. 92:883-893; Ishibashi et al., 1994, J. Clin. Invest. 93:1885-1893) was studied. LDL receptor-deficient mice have elevated LDL cholesterol relative to wild type mice when fed a chow diet. When fed cholesterol-enriched diets, these mice develop atherosclerosis.

Detailed Description Text (310):

FIG. 17 shows the lipoprotein cholesterol profiles (Bisgaier et al., J. Lipid Res. 38:2502-2515) of 4 chow-fed female LDL receptor deficient mice prior to and following therapy with 300 mg/kg/day of Compound A. All mice showed a rapid and significant reduction in LDL cholesterol after one week of treatment. In addition, FIG. 17 shows that Compound A caused HDL elevation in all treated mice.

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